UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,328	01/23/2001	Satoshi Sasaki	Q62621	4446

7590 07/30/2003

Sughrue Mion Zinn Macpeak & Seas
Suite 800
2100 Pennsylvania Avenue NW
Washington, DC 20037-3213

EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 07/30/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/744,328	SASAKI ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-12,17,19-22,25 and 29-35* is/are pending in the application.

4a) Of the above claim(s) *5,7-10,17,19-22,29 and 31-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,6,11,12,25,30 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2,11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

1. Claims 1, 3, 5-12, 17, 19-22, 25 and 29-35 are pending.

Applicants' amendment filed May 27, 2003 (Paper No. 11) is acknowledged. Applicants' response has been fully considered. Claims 5, 7-10, 17, 19-22, 29 and 31-34 are non-elected invention and stand withdrawn from consideration. Claims 1, 6, 11, 25 and 35 have been amended, and claims 2, 4, 26-28 and 36 have been cancelled. Thus, claims 1, 3, 6, 11, 12, 25, 30 and 35 are examined.

2. The drawings filed January 23, 2001 have been approved by the draftsman.

3. The references listed on PTO-1449 filed January 23, 2001 have been considered, and an initialed copy of PTO-1449 is attached.

Objection Withdrawn

4. The previous objection of claims 6 and 11 is withdrawn in view of applicants' amendment to the claims, and applicants' response at page 4 in Paper No. 11.

Rejection Withdrawn

Claim Rejections - 35 USC § 112

5. The previous rejection of claims 1-4, 6, 11 and 12, under 35 U.S.C.112, first paragraph, regarding the claim recitation of the activity of galectin-3 as the function of the compound, is withdrawn in view of applicants' cancellation of the claim, applicants' amendment to the claim, and applicants' response at pages 4-5 in Paper No. 11.

6. The previous rejection of claims 1-4, 6, 11, 12, 25, 27, 30, 35 and 36, under 35 U.S.C.112, second paragraph, regarding the claim recitation of the activity of galectin-3 as the

function of the compound, insufficient antecedent basis, and "the biological activity of galectin-3" not cited in the claim, is withdrawn in view of applicants' cancellation of the claim, applicants' amendment to the claim, and applicants' response at page 8 in Paper No. 11.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 3, 6, 11, 12, 25, 30 and 35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition comprising an identified compound such as LNFP-I that inhibits the biological activity of galectin-3, which promotes the production of extracellular matrix from an extracellular matrix-producing cell; or a method for inhibiting the overproduction and accumulation of extracellular matrix, comprising administering an identified compound that inhibits the binding of galectin-3 to the extracelluler matrix in the extracelluler matrix-producing cells, does not reasonably provide enablement for a pharmaceutical composition having inhibitory effect on glomerular nephritis, diabetic nephropathy or tissue fibrosis comprising a compound that inhibits the biological activity of galectin-3; or a method for inhibiting glomerular nephritis, diabetic nephropathy or tissue fibrosis caused by the overproduction and accumulation of extracellular matrix, comprising administering a compound having an inhibitory effect on the biological activity of galectin-3 to a subject, where the compound is not defined. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1, 3, 6, 11, 12, 25, 30 and 35 are directed to a pharmaceutical composition having inhibitory effect on glomerular nephritis, diabetic nephropathy or tissue fibrosis comprising a compound that inhibits the biological activity of galectin-3 (claims 1, 3, 6, 11, 12); or a method for inhibiting glomerular nephritis, diabetic nephropathy or tissue fibrosis caused by the overproduction and accumulation of extracellular matrix, comprising administering a compound having an inhibitory effect on the biological activity of galectin-3 to a subject (claims 25, 30 and 35). The specification, however, only discloses cursory conclusions without data supporting the findings, which states that the compounds that inhibit the biological activity of galectin-3 can be used as a therapeutic or preventive agent for glomerular nephritis, diabetic nephropathy or tissue fibrosis which is caused by the overproduction and accumulation of extracellular matrix (page 5, lines 3-8). There are no indicia that the present application enables the full scope in view of a pharmaceutical composition comprising a compound that inhibits the biological activity of galectin-3, and a method for inhibiting glomerular nephritis, diabetic nephropathy or tissue fibrosis using an inhibitor of galectin-3 as discussed in the stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breath of the claims, the absence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breath of the claims:

The breath of the claims is broad and encompasses unspecified variants regarding the compounds that inhibit the biological activity of galectin-3, and the treating conditions for inhibiting the cited diseases, which are not adequately described or demonstrated in the specification.

(2). The absence of working examples:

There are no working examples indicating the claimed methods in association with the variants except for certain compounds such as fetuin glycoprotein and LNFP-1 which inhibit galectin-3 binding and the promotion of collagen type IV production in rat mesangium cells (Examples 5 and 6).

(3). The state of the prior art and relative skill of those in the art:

The prior art indicates galectin-3 binds to a sugar chain of glycoprotein present on the cell surface or in the extracellular matrix that activates inflammatory cells (page 1, lines 21-32 of the specification), and the overproduction and accumulation of extracellular matrix such as collagen is believed to be an important factor for the pathogenesis of the fibrosis of tissues (page 2, lines 5-13). However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the compounds inhibiting the biological activity of galectin-3 and the treating conditions for inhibiting the cited diseases to be considered enabling for the claimed method.

(4). Predictability or unpredictability of the art:

The specification has shown galectin-3 is involved in the formation of fibrosis or nephritis in rat model (Examples 1 and 2), galectin-3 has promoting effect on the collagen type IV production in mesangium cells (Example 4), and fetuin glycoprotein and LNFP-1 which

inhibit galectin-3 binding, also inhibit the promotion of collagen type IV production in rat mesangium cells (Examples 5 and 6). However, the specification does not provide the use of compounds that inhibit the biological activity of galectin-3 in inhibiting glomerular nephritis, diabetic nephropathy or tissue fibrosis, the invention is highly unpredictable regarding the effects of the compounds.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a pharmaceutical composition having inhibitory effect on glomerular nephritis, diabetic nephropathy or tissue fibrosis comprising a compound that inhibits the biological activity of galectin-3, and a method for inhibiting glomerular nephritis, diabetic nephropathy or tissue fibrosis, comprising administering a compound having an inhibitory effect on the biological activity of galectin-3 to a subject. Although galectin-3 has been shown to be involved in the formation of fibrosis or nephritis in rat model (Examples 1 and 2), and galectin-3 has promoting effect on the collagen type IV production in mesangium cells (Example 4), the specification only indicates certain compounds such as fetuin glycoprotein and LNFP-1 which inhibit galectin-3 binding also inhibit the promotion of collagen type IV production in rat mesangium cells (Examples 5 and 6). The specification has not demonstrate a specific compound that inhibits the biological activity of galectin-3 also inhibits glomerular nephritis, diabetic nephropathy or tissue fibrosis. There is no working example indicating such treatment. The specification has not provided the treating condition such as the dose, the time and the effect of a specific galectin-3 inhibitor in treating the cited diseases. Furthermore, there is no data indicating the *in vitro* effect can be applied to *in vivo* model. Since the specification fails to

provide sufficient guidance on the use of various galectin-3 inhibitors in treating the cited diseases, it is necessary to carry out further experimentation to assess the in vivo effects of these compounds.

(6). Nature of the Invention

The scope of the claims encompass using galectin-3 inhibitor for inhibiting glomerular nephritis, diabetic nephropathy or tissue fibrosis, but the specification does not provide sufficient teachings on the use and the effects of compounds in inhibiting the cited diseases. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, the working example does not demonstrate the claimed methods associated with the variants, the art is unpredictable regarding the effects of the compounds, and the teaching in the specification are limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the inhibitory effect of the compound in treating glomerular nephritis, diabetic nephropathy or tissue fibrosis in vivo.

In response, applicants indicate it is known in the art that an accumulation of extracellular matrix (ECM) causes the diseases cited in the claim such as glomerular nephritis, diabetic nephropathy or tissue fibrosis, and the specification has shown galectin-3 promotes the accumulation of type IV collagen, which represents ECM, therefore, it is reasonable to expect that a substance that inhibits the activity of galectin-3, also inhibits these diseases; This expectation is supported by the references (Shimizi et al., 1997, 1998; Al-Bayati et al., 2002, provided by applicant), which indicate a compound "pirferidone (PFD)" inhibits the production and accumulation of collagen that is in extracellular matrix, and in various models PFD inhibited the overproduction of collagen IV and alleviated chronic renal disorders, therefore, one or

ordinary skill in the art would expect that compounds that inhibits the overproduction and accumulation of ECM promoted by galectin-3 would be useful to treat diseases caused by such overproduction and accumulation of ECM; and regarding the scope of galectin-3 inhibitors, the specification (pages 6-8) has described numerous ways to inhibit the activity of galectin-3, and substances that inhibit galectin-3 can be easily selected using conventional screening method for galectin-3, thus, one skilled in the art knows how to identify appropriate compounds useful in the claimed method (pages 5-7 of the response). Applicants' response has been fully considered, however, the argument is not found persuasive because the specification has not shown the correlation between in vitro data and the in vivo effect, and how to apply the in vitro data to in vivo effect, thus without further experimentation it is not known whether these compounds would be effective in treating the cited diseases in vivo, even though the specification has shown certain compounds such as fetuin glycoprotein and LNFP-1 inhibit the promotion of collagen type IV production in rat mesangium cells. Regarding the compound "PFD", since PFD has very different structure from a galectin-3 binding inhibitor such as some sugars (listed at page 6 of the specification), and the references do not indicate PFD is a galectin-3 inhibitor, thus, the in vivo effect of PFD in treating renal disorders would not be expected in the compounds of galectin-3 inhibitors. Regarding identifying a galectin-3 inhibitor used for the claimed method, since there are many galectin-3 inhibitors with diverse structures, and the specification has not provided sufficient teachings on the use of various galectin-3 inhibitors in treating the cited diseases, nor indicating and the effects of these inhibitors, thus, it is necessary to have additional guidance and to carry out further experimentation to assess the inhibitory effects of these compounds in treating cited diseases.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 25, 30 and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 25, 30 and 35 are indefinite because they lack essential steps as claimed in the method for inhibiting glomerular nephritis, diabetic nephropathy or tissue fibrosis in a subject. The omitted step is the outcome of the process. Claims 30 and 35 are included in the rejection because they are dependent on a rejected claim and do not correct the deficiency of the claim from which they depend.

Conclusion

9. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

***
July 29, 2003

Christopher S.F. Low
CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600